

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

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|--|--|--|---|
| | | | Date of mailing (day/month/year) see form PCT/ISA/210 (second sheet) |
| Applicant's or agent's file reference see form PCT/ISA/220 | | FOR FURTHER ACTION See paragraph 2 below | |
| International application No. PCT/EP2004/006592 | International filing date (day/month/year) 17.06.2004 | Priority date (day/month/year) 19.06.2003 | |
| International Patent Classification (IPC) or both national classification and IPC A61K31/4025, C07D409/12, C07D409/14, C07D413/14, A61P7/02 | | | |
| Applicant GLAXO GROUP LIMITED | | | |

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

| | |
|--|---|
| Name and mailing address of the ISA: | Authorized Officer |
|  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | Cortés, J Telephone No. +49 89 2399-8206 |
|  | |

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/EP2004/006592**IAP20 Rec'd PCT/EP/TO 19 DEC 2005****Box No. I Basis of the opinion**

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material:

a sequence listing
 table(s) related to the sequence listing

b. format of material:

in written format
 in computer readable form

c. time of filing/furnishing:

contained in the international application as filed.
 filed together with the international application in computer readable form.
 furnished subsequently to this Authority for the purposes of search.

3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/006592

Box No. II Priority

1. The following document has not been furnished:

copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).
 translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/006592

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

the entire international application,
 claims Nos. 10

because:

the said international application, or the said claims Nos. 10 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 no international search report has been established for the whole application or for said claims Nos.
 the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form has not been furnished

does not comply with the standard

the computer readable form has not been furnished

does not comply with the standard

the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/006592

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | |
|-------------------------------|-------------|--------|
| Novelty (N) | Yes: Claims | 1-11 |
| | No: Claims | |
| Inventive step (IS) | Yes: Claims | 1-11 |
| | No: Claims | |
| Industrial applicability (IA) | Yes: Claims | 1-9,11 |
| | No: Claims | |

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

10/561545

IAP20 Rec'd PCT/PTO 19 DEC 2005

International application No.

PCT/EP2004/006592

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 10 relateS to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion with regard to the industrial applicability will be formulated for this claim (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The following document has been cited in the International Search Report:

D1: WO 03/043981 A (GLAXO (GB)) 30 May 2003 (2003-05-30)

Novelty (Article 33(2) PCT)

The present compounds differ from the compounds in D1 in the groups X and R2.

Inventive Step (Article 33(3) PCT)

D1 discloses factor Xa inhibitors and can be regarded as the closest prior art.

The problem of the invention was the provision of new factor Xa inhibitors.

D1 does not suggest the substitution of the pyrrolidones disclosed therein with a phenyl or a heterocyclic group in position 1.

The present invention is therefore based on an inventive step.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2004/006592

Re Item VI

Certain documents cited

The following P-document has been cited in the International Search Report:

D2: WO 03/053925 A (GLAXO (GB)) 3 July 2003 (2003-07-03)

The priority documents pertaining to the present application were not available at the time of establishing this report. Hence, it is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct, the P-document D2 cited in the international search report could become relevant to assess whether the present claims satisfy the criteria set forth in Article 33(1) PCT.

The proviso for R2 seems to have the function to delimit the application from D2. However there seems to be a mistake ("C2-3" instead of "C1-3"). Consequently there is still an overlap for "C1-alkyl-morpholino".